

Acute Encephalitis Syndrome in India: Current Issues and Challenges

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Abstract

AES was a term introduced in 2008 by the World Health Organization to strengthen the surveillance and research of AES in India. AES is characterized by high case fatality rate particularly of children below 15 years. Clinically presents with fever and altered consciousness and rapid worsening of the condition often leading to death. Japanese encephalitis virus (JEV) is the leading diagnosed cause of acute encephalitis, other causes include enteroviruses, scrub typhus, and other viruses circulating in the local area. In many cases, however, no etiological agent is determined, and such cases are categorized broadly as acute encephalitis syndrome (AES). It has been in recent years a pressing public health emergency in India.

Keywords: Encephalitis; Syndrome; fatality; neurologic.

Introduction

Acute Encephalitis Syndrome (AES) manifests with a wide group of neurologic manifestation caused by a wide range of viruses, bacteria, fungus, parasites, spirochetes, chemical and toxins. AES is reported mainly from Assam, Bihar, Karnataka, Uttar Pradesh and Tamil Nadu which contributes

approximately 80% of cases and has high case fatality rate reported almost every year.

History

The history of AES has been classified based on various surveillance reports and outbreak of the first phase being prior to 1975 when there were a few cases. The second phase between 1975 and 1999 when there were more cases reported particularly in the Gangetic plains and the third phase from 2000 to 2010 which saw the emergence of many other causes of AES other than Japanese Encephalitis which included viruses like Chandipura virus and Nipah virus [2].

Several endemic regions of various viruses reported to cause AES in India. JEV has its endemic zones running along the Gangetic plane including states of UP (east), Bihar, West Bengal and Assam, and parts of Tamil Nadu.

Chandipura virus on the other hand made its arrival in Maharashtra and Eastern Gujarat in 2003 but also has seen activity in Andhra Pradesh. Nipah virus hit the south-east Asian countries, mainly Bangladesh. It had its first outbreak in Siliguri, West Bengal in 2001. Nipah virus again caused

an outbreak in Nadia district of West Bengal in 2007 and more recently in 2018 in Kerala and also 2019 again in Kerala. The so called Litchi virus was the latest virus in the list that caused AES in Muzzafarpur, Bihar and Malda, West Bengal from 2013 to 2014.

Definition

Acute encephalitis defined as the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk), and/or new onset of seizures (excluding simple febrile seizures).

Japanese encephalitis is vector borne disease that is usually spread by Culex mosquitoes and the transmission cycle is maintained by mosquitoes, pigs and Ardeid birds.

Prevalence

The outbreak of JE usually coincides with the monsoon and post monsoon period when the density of mosquitoes increases while encephalitis due to other viruses specially enteroviruses occurs throughout the year. The case fatality and morbidity is very high among various viral encephalitis specially in JE or entero virus encephalitis in various parts of India.

The first reported Japanese encephalitis was reported from Vellore in Tamil Nadu in 1955. Subsequently the first outbreak was reported from Bankura in West Bengal in 1973 [1]. Since then there have been several sporadic outbreaks across India. Thereafter, sporadic cases of AES and outbreaks have been the leading cause of premature deaths due to the disease in India.

AES in Gangetic belt

Between 2008 and 2014, there have been more than 44,000 cases and nearly 6000 deaths from encephalitis in India, particularly in Uttar Pradesh and Bihar. In 2016, there has been a rise in encephalitis, with over 125 children deaths in one hospital in Gorakhpur, Uttar Pradesh alone. Gorakhpur had successive outbreaks in 2005, 2006 and 2007 and also in 2017.

In 2006 there were 6061 cases with 15000 deaths while in 2007 there were 2320 cases with 528 deaths and in 2007 there were 3024 cases and 645 deaths with 1500 deaths. It was followed by further outbreaks

in 2006 and 2007, with 2320 cases and 528 deaths and JEV was identified as the causative agent in some cases, while in some studies, besides scrub typhus *Enterovirus* was identified as the infective agent. This led to India launching a JE vaccination programme in 2006, which in 2014 became part of the National immunization programme [13]. The programme now makes the vaccine available in 179 districts in nine States where the disease is highly prevalent. Epidemics of encephalitis of unknown aetiology have occurred in the country.

Epidemiology

The neighbouring State of Bihar, particularly Muzaffarpur district, has been reporting cases of acute encephalitis among children since 1995. In 2011, there were 147 cases and 54 deaths (CFR 36.7%) in the district. In the following year, 469 cases and 178 deaths were reported from health facilities with CFR of 38.6 per cent [14].

Agent

Litchi is a fruit belonging to the soapberry family and is found mainly in India and China. In 1962, it was found that lychee seeds contained methylene cyclopropylglycine (MCPG), a homologue of hypoglycin A, which caused hypoglycemia in animal studies. Unripe fruit contain the toxins hypoglycin A and methylene cyclopropyl glycine (MCPG), which cause vomiting if ingested in large quantities. Hypoglycin A is a naturally occurring amino acid found in the unripe litchi that causes severe vomiting quite similar to what occurred in Jamaica after eating unripe ackee fruits (Jamaican vomiting sickness).

Host

The age of the hospitalized cases ranged from six months to 16 yr with 92 per cent below the age of 10 yr. [2]. In 2018 again there were more than 125 deaths from Muzaffarpur alone [3].

Clinical Manifestation

The clinical presentation in the Muzaffarpur epidemic included sudden onset of convulsions with clenching of teeth and loss of consciousness, mostly in the early morning, with no prodrome or sequelae. Many of them did not have fever.

Hypoglycaemia was a common feature (50% of the observed cases). The serum and cerebrospinal fluid examinations were, however, inconclusive. On an average, one case was seen per village. All cases occurred during May and June, which coincided with the litchi plucking season in the district.

While MCPG is a poisonous compound found in litchi seeds that causes a sudden drop in blood sugar, vomiting, altered mental states leading to lethargy, unconsciousness, coma and death. These toxins cause sudden high fever and seizures serious enough to require hospitalisation in young, severely malnourished children. It is postulated that eating of unripe fruits on an empty stomach in children leads to this disease.

Issues and Challenges

There are many causes of AES while Japanese encephalitis was a major cause of AES it is now the only cause. However, since it is a major cause, vaccination of all children in endemic zones 181 districts have been brought under this scheme.

In Gorakhpur in Uttar Pradesh in addition to Japanese Encephalitis scrub typhus caused by Oriental mite *Orientia Tsutsugamushi* is a major cause [4,5]. While the vaccination campaign against Japanese encephalitis by the Government of India has reduced the number of cases to a large extent. lot more needs to be done regarding the occurrence of scrub typhus.

In the very recent Muzaffarpur outbreak of 2019 killing more than 121 children. Some studies point to the possible link with litchi fruits in Muzaffarpur, Bihar, since the outbreaks occur in litchi fruit growing region in India, and cases tend to peak during litchi harvesting season Besides India, outbreak reports from Vietnam and Bengal also suggest that litchi-associated encephalitis can occur following consumption of litchi fruits, which contains hypoglycin A and methylene cyclopropylglycine (MCPG) [3,6,7].

However a study from Bangladesh suggests that it is not litchi but pesticides sprayed on it that cause the disease [8]. Among the pesticides mentioned in the study in Bangladesh are cypermethrin, endosulfan.

Other causes attributed to Muzaffarpur outbreak also include lack of evening meal, and malnutrition and the extreme heat.

While there were recommendation for children to have their evening meals before sleeping but this

was not followed. However there is no evidence of malnutrition in Muzaffarpur being higher than the rest of Bihar.

Conclusion and Recommendations

There are several causes of AES and several risk factors. While in Gorakhpur Uttar Pradesh scrub typhus has been proven to be a a major cause in addition to Japanese encephalitis the situation is different in Muzaffarpur in adjoining Bihar where consumption of lytchee fruit along with malnutrition and extreme heat have been suggested as possible factors [10,11].

While vaccination can reduce the burden of Japanese encephalitis, environmental control is also needed to reduce incidence of scrub typhus and other vector borne diseases [10].

Good nutrition and health education in addition to strengthening infrastructure is also the need of the hour. While the role of pesticides is not confirmed it may be useful to check their toxicity if any.

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